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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/125,747	08/25/98	TOROSSIAN F	TORO-0101-PU

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1645	15

DATE MAILED: 11/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/125,747	Applicant(s) Torossian
	Examiner S. Devi, Ph.D.	Group Art Unit 1645

☒ Responsive to communication(s) filed on *08/15/00.*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *9-16* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *9-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *11.*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Applicant's Amendments

1) Acknowledgment is made of Applicant's amendments filed 06/26/00 and 08/14/00 (paper no. 12 and 13). With these, Applicant has amended the specification.

Priority Document

2) Acknowledgment is made of Applicant's submission of the priority document 96 02445 filed 02/26/96 in France.

Status of Claims

3) Claims 1-8 have been canceled via the amendment filed 06/26/00.

New claims 9-16 have been added via the amendment filed 06/26/00.

Claims 9-16 are pending and are under examination.

Supplemental Information Disclosure Statement

4) Acknowledgment is made of Applicant's supplemental information disclosure statement filed 06/26/00 (paper no.11). An initialed copy is attached to this Office Action (paper no. 15). The IDS requests the Office to consider an US application, SN 08/387,322 with the Applicant's name listed as Torossian. However, the Office does not appear have such an application wherein Torossian is the inventor. Therefore, the citation on Applicant's IDS has been lined through.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Specification/Informality

7) The abstract submitted by the Applicant on 06/26/00 is objected to because the first

sentence of the abstract is not complete and is inconsistent with the first sentence of the published abstract of PCT/FR97/00334. Applicant states that "the enclosed Abstract is the same as PCT/FR97/00334" (see page 7 of Applicant's amendment filed 06/26/00). However, as pointed above, the submitted abstract is not the same as the one printed in PCT/FR97/00334. Correction is requested.

Objection(s) Withdrawn

8) The objection to the specification made in paragraph 7 of the Office Action mailed 12/22/00 (paper no. 8) is withdrawn in light of Applicant's amendment to the specification.

9) The objection to the specification made in paragraph 8 of the Office Action mailed 12/22/00 (paper no. 8) is withdrawn in light of Applicant's amendments to the specification.

Objection(s) Moot

10) The objection to claims 1 and 3-7 made in paragraph 14 of the Office Action mailed 12/22/00 (paper no. 8) is moot in light of Applicant's cancellation of the claims.

Rejection(s) Moot

11) The rejection of claims 1-8 made in paragraph 10 of the Office Action mailed 12/22/00 (paper no. 8) under 35 U.S.C. § 112, first paragraph, as being non-enabled, is moot in light of Applicant's cancellation of the claims.

12) The rejection of claims 1-8 made in paragraph 13 of the Office Action mailed 12/22/00 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claims.

Applicant's Arguments & Office's Response

13) Applicant contends that the claims of the present application are sufficient to allow persons skilled in the art to make and use the invention (see page 8 of Applicant's amendment filed 06/26/00). Applicant points to page 1, lines 1-7 and state that the claimed complex has "a specific action against *Helicobacter* (former *Campylobacter*) by means of RNA of ribosomal origin extracted specifically form the bacteria of claim 1". However, contrary to the Applicant's contention, lines 1-7 of page 1 of the instant specification does not mention about "RNA of

ribosomal origin extracted specifically form the bacteria of claim 1". New claims of the present application are also insufficient to allow those skilled in the art to practice the invention as claimed.

With regard to the double effect (therapeutic and preventive) of vaccination, Applicant states that "both preventive and therapeutic" effect of vaccination is known to persons of skill in the art, because the definition of "vaccine" in *Dorland's Medical Dictionary*, page 1787, 28th Edition (Exhibit A). The definition of "vaccine" from the Dictionary is as follows:

> ...a suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), or of antigenic proteins derived from them, administered for the prevention, amelioration, **or** treatment of infectious diseases. [Emphasis added].

As is clear from the definition for "vaccine" provided by Applicant himself/herself, a vaccine comprising a suspension of attenuated or killed bacteria, viruses or rickettsiae, or antigenic proteins derived from them, is administered for the preventive **or** therapeutic effect, and not for both preventive and therapeutic effect, as is incorrectly interpreted by the Applicant. Thus, the Applicant's contention that "therapeutic complex" and "vaccine complex" are used with the same meaning appears to be incorrect.

With regard to the recitation "functional arm and genetic arm" in the base claim, the Applicant submits the reference of Gerald Joyce (Exhibit B). This reference is in a non-English language with which the Examiner is not versed in. Applicant states on page 10 of his/her amendment that a small relevant part of the publication on page 77 is translated to English. However, the translation is grammatically poor with incomplete sentences, and the Office is unable to understand the relevance of this part of the prior art disclosure to the instant invention, without proper translation of the whole document. Since the therapeutic or preventive potential of the dual molecules mentioned in the translated portion and their source is unknown, one of ordinary skill in the art would not be able to understand their relevance to the instant invention and would not be able to practice the instant invention based on what is translated, without undue experimentation.

Applicant cites a part of page 13 of a 1991 Oxford Medical Publications (Exhibit C) which

provides the general definition of "epitope", "idiotype" and "anti-idiotype". However, it is not clear how this general definition is related to the "ability to limit the proliferation and further differentiation" making it possible to "avoid recidivations of the initial digestive tract pathology" as claimed in claim 13. Claim 13 vaguely and/or broadly recites "anti-bacterial antibodies" and does not even disclose the aetiology of the recited "recidivations of the initial digestive tract pathology".

On page 14 of the amendment filed 06/26/00, Applicant states that the "complex of claim 9 contains two types of elements, i.e., bacterial membrane fractions and ribosomal RNA originating from defined bacteria" and that the "two types of elements induce immunological responses that are directed against the different micro-organisms". Applicant further states that the association of multiple immunological stimulating elements is a reason for the success of the complex to "avoid recidivations of the initial pathology". However, what is recited in claim 9 does not convey this. Element (a) of the vaccine complex of claim 9, as drafted currently, neither comprises bacterial membrane fractions, nor ribosomal RNA of bacterial origin. There is no disclosure indicating that element (a) of the vaccine complex induces immunological responses that are directed against any microorganism, or that "avoid recidivations of the initial pathology".

New Rejection(s)

Applicant is asked to note the new rejections made in this Office Action. The Applicant's amendment, i.e., the addition of new claims, necessitated the new ground(s) of rejection presented in this Office Action.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

14) Claims 9-16 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400

(Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

The specification fails to set forth sufficient evidence showing that the claimed vaccine complex could be made and used with "dual molecules" of part (a) of claim 9 comprising **any** "functional amino acid arm" and **any** "genetic ribonucleic acid arm". As drafted currently, infinite functional amino acid arms and infinite genetic ribonucleic acid arms are included in the scope of the claim(s), but no guidance has been provided as to their source and as to how they are produced. Furthermore, the immunologic and biologic specificity of these two arms and the precise mechanism by which these unspecified "arms" accomplish the alleged results, i.e., of being effective against "antibiotic resistant bacteria", "recidivations of the initial digestive tract pathology" of unknown aetiology and "*Helicobacter* generating pathogeneses", is undisclosed. The aetiology (i.e., microbial or bacterial or non-microbial or auto-immune) of the "recidivations of the initial digestive tract pathology" is neither recited in claim 13 or claim 15, nor described in the specification. There is no evidence that the subjects of Examples 2-4, who were treated with the complex of the instant invention, were effectively treated against *Helicobacter*-induced gastritis or duodenal ulcer, because there is no disclosure about the actual aetiology of gastritis or duodenal ulcer in these subjects. Further, which resistant bacteria, among a myriad of bacteria are encompassed in the scope of claim 14, the vaccine complex is effective against.

Claim 12, which depends from claim 9, 10 or 11, recites the immunomodulatory and vaccine complex of the instant invention for use in the treatment of diseases caused by *Helicobacter* bacteria "by the production of antibodies". However, the specification on page 3, lines 3 and 4, states the "inefficacy" of the *Helicobacter*-specific antibodies in protecting an

individual.

The specification does not enable a vaccine comprising the components recited in part (a) of claim 9. Instant specification does not provide a clear written description of "a functional amino acid arm, ensuring binding to a target, with a genetic RNA arm corresponding to the coded description of the composition of the functional arm" (claim 9). Whether or not these components are of bacterial or non-bacterial origin is not disclosed. Further, the precise description or meaning and scope of "factors linked to the bacterium" and "factors linked to the host" recited in claim 15 is difficult to envisage. On page 15 of the amendment filed 06/26/00, Applicant describes substances secreted by the bacterium, for example cytotoxins, as factors related (linked) the bacterium. However, the art recognizes that cytotoxin-directed immunity is specific. It is not understood how the vaccine complex of the instant invention (which does not contain cytotoxin-related antigens) induces cytotoxin-specific immune response.

Furthermore, page 13 of the specification recites collagen type III as the "immunity adjuvant factor", and the complex as containing "amino acid sequences" of the collagen type III. However, claim 11 recites that the amino acids from collagen are selected from the various amino acids recited in the claim. The collagen type III is stated on page 13 to be characterized by "Amino acid sequences similar to" the "sequence" shown on page 13, wherein several individual amino acid residues are recited one below the other. No amino acid sequences are provided or identified specifically by a SEQ ID number. It is unclear what Applicant means by amino acid sequences "similar" to the "following sequence". It is unclear how one determines which amino acid "sequences" are similar to the individual amino acids (not sequences) recited on page 13. With this description, one of ordinary skill in the art would not be able to understand whether the whole sequence is present in the complex, or any one of the recited amino acids is included in the complex, or a mixture of any of these amino acids is included in the complex, and therefore would not be able to make and use and/or reproducibly practice the invention without undue experimentation.

Further, the specification does not allow one of ordinary skill in the art to grasp the nature

of the association between the multiple components present in the "complex". For example, the optimal amounts or proportions of different "bacterial membrane fractions" , i.e., glycopeptides and/or lipopolysaccharides and the ribonucleic acid arm, that should be present in the complex such that the complex can accomplish its alleged therapeutic and/or preventive functions are not disclosed. On page 14 of the specification, it is stated that the vaccine complex of the invention is produced by "combining ribosomal RNAs or RNA fragments, membrane fractions (for example proteoglycans from *Klebsiella pneumoniae*) and collagen type III...." to "obtain a high level of protection and of cure". Neither the source of ribosomal RNAs, RNA fragments, or the recited collagen, nor the nature of the antibiotic resistant disease or the antibiotic resistant bacteria against which it supposedly produces high level cure or protection is disclosed. The precise source (species-wise) of the broadly recited "functional amino acid arm" and of "genetic ribonucleic acid arm" recited in component (a) of claim 9 is not understood. In component (a) of claim 9, it is also unclear binding to what target is being ensured by covalent coupling of a functional amino acid arm with a genetic ribonucleic acid arm. One of ordinary skill in the art would not be able to practice the invention as claimed without undue experimentation.

In sum, the actual invention is not described in such a way that one skilled in the art could grasp the invention and make and use the invention and/or reproducibly practice the invention with a reasonable expectation of success, without undue experimentation. The breadth of instant claims is not commensurate in scope with the enabling disclosure or evidence. In the absence of specific guidance and evidence, instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

15) Claims 9-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claim 9 is drawn to a vaccine complex comprising component (a) and component (b). As drafted currently, both components include a ribonucleic acid arm. The ribonucleic acid

arm of component (b) is recited to be extracted from the recited bacterium or bacteria. Part (a) of claim 9 includes "a functional amino acid arm" covalently coupled to a "genetic ribonucleic acid arm corresponding to the coded description of the composition of the functional arm". However, the origin or the source of these two "arms" from part (a) is unclear. Claim 9 is vague and confusing in the recitation of "a genetic ribonucleic acid arm" in part (a) and "the ribonucleic acid arm" in part (b) of claim 9. Do the ribonucleic acid arms from part (a) and (b) represent two distinct ribonucleic acid arms, the one from part (b) of *Helicobacter* origin and the one from part (a) of a non-specific or non-*Helicobacter* origin?

(b) Claim 13 is vague and indefinite in the recitation "avoidance ..... are avoided". It is unclear what Applicant means by this.

(c) Claim 13 is vague and indefinite in the recitation of idiotype of "anti-bacterial" antibodies, because it is unclear antibodies to what bacteria Applicant is referring to. Further, it not clear "recidivations of the initial digestive tract pathology" caused by what microbe or bacterium is being avoided.

(d) In Claim 9, part (b), proper antecedence appears to be lacking for the recitation "the ribonucleic acid arm", because the earlier recitation in the claim is to "a genetic ribonucleic acid arm" pertinent to the dual molecules of part (a) of the claim, and not pertinent to the bacterial membrane fractions of part 9(b).

(e) In claim 9, "the functional arm" in the last line of part (a) lacks antecedent basis, because the earlier recitation in part (a) of the claim is to a "functional amino acid arm".

(f) Claim 9 is vague and indefinite in the recitation: "a genetic ribonucleic acid arm corresponding to the coded description of the composition of the functional arm", because it is unclear what Applicant means by "the coded description". It is not understood which functional arm Applicant is referring to. How does one identify that an "arm" is "functional"? Functional in what sense?

(g) Claim 12 depends from claim 9, the vaccine complex of which comprises dual molecules of unspecified sources and bacterial membrane fractions and ribonucleic acid arm of

ribosomal origin from selected species of *Helicobacter*, or from unspecified species of *Campylobacter*. What is the specificity of the antibodies? Are these antibodies specific to dual molecules or to the part (b) components?

(h) Claim 9 appears to be redundant in the recitation of *Helicobacter* species and *Campylobacter*, because on page 9 of their amendment filed 06/26/00, Applicant refers to *Helicobacter* as "former *Campylobacter*".

(I) Claim 14 is vague in the recitation "antibiotic-resistant bacteria", because it is unclear which antibiotic-resistant bacteria Applicants are referring to. It is unclear how a vaccine made of components (a) and (b) of the base claim can be used against any unspecified "antibiotic-resistant bacteria".

(j) Claim 15 lacks antecedent basis for the recitation "the formulation" (see line 2). Claim 15 depends from one of claims 9-11, none of which recite any "formulation".

(k) Claim 15 is vague and indefinite in the recitation "major" anti-inflammatory agents (lines 4 and 5), because "major" is a relative term and it is unclear what is encompassed in this limitation.

(l) Claim 15 is vague and indefinite in the recitation "*Helicobacter* generating pathogeneses", because it is unclear what Applicant means by this. Does Applicant mean to say --*Helicobacter*-generated pathogeneses--?

(m) Claim 15 is vague and indefinite in the recitation "products with bactericidal effect and products with bacteriolytic effect" (lines 6 and 7), because it is unclear how these products differ from one another. What are the differences between the two products, if any?

(n) Claim 15 lacks antecedent basis for the recitation "the bacterium" (lines 8 and 9), because there is no earlier recitation of any "bacterium" in claim 15, or in the claim from which it depends.

(o) In claim 15, what is meant by "Helicobacter generating pathogeneses by factors linked to bacterium" or "by factors linked to the host"? What "factors" are linked to what bacterium or what host, and how are they linked?

(p) Claim 15 lacks antecedent basis for the recitation "the host" (see last two lines), because there is no earlier recitation of any "host" in claim 15 or in the claim from which it depends.

(q) Claim 16 lacks antecedent basis for the recitation "said formulation" (see line 2). Claim 15 depends from one of claims 9-11, none of which recite any "formulation".

(r) Claim 16 is vague and confusing in the recitation: "route selected from ..... infusions....injections.....devices", because injections and devices do not constitute "routes".

(s) Claims 10-16, which depend directly or indirectly, from claim 9 are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite, because of the defects identified above in subparagraphs (a) through (q).

Objection(s)

16) Claim 15 is objected to for the following reasons:

(a) Claim 15 is incorrect in the recitation "the said" complex (see lines 2 and 3). It is suggested that Applicant use one of the terms.

(b) Claim 15 is objected for the use of vague and/or superfluous claim language, such as, mediators "like", "such as various", "factors linked to the bacterium" and "factors linked to the host".

Remarks

17) Claims 9-16 stand rejected.

18) **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

20) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 a.m to 4.00 p.m. A message may be left on the Examiner's voice mail service.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. Devi
Patent Examiner
November 2000

L. F. Smith
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